How Can Statistical Approaches Be Used To Link PM Components With Health Effects?

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research and development

Introduction

- One way to regulate PM would be to regulate sources which emit particles instead of treating all particles as if they were of equal toxicity regardless of their source of origin.
- Two different approaches are currently being used to identify health effects associated with specific sources. One involves exposure to PM enriched for a specific source, a so-called "bottom up" approach. The most common bottom up approach is to use pre-collected source materials in inhalation, instillation, and in vitro studies to define toxicity of these materials.
- Another approach is to expose humans or animals to ambient PM and use comprehensive monitoring of pollutants together with statistical approaches to define common source components.
- The most common "top down" approach is to expose humans or animals to CAPs followed by determination of the correlation of source components to observed responses.
- In this poster, statistical approaches to define the correlations between components in ambient particle exposures and adverse outcomes are explored.

Research Goal

To use statistical methodology to link biological effects with PM components, and ultimately sources, in humans and animals exposed to ambient PM.

Methods/Approach

Statistical approaches for analyses of ambient exposure studies and CAPs experiments include:

1. Binary comparisons of outcomes, exposed vs not exposed, CAPs vs Sham, with t/f test based analyses;
2. Simple linear regression analyses, ambient/CAPs mass or measured ambient/CAPs component versus measured outcomes;
3. Multivariate regression analyses, ambient/CAPs mass or measured ambient/CAPs components as tracers of sources versus measured outcomes;
4. Multivariate regression analyses using reconstructed source contributions based on principal component analyses (factor analyses) versus measured outcomes;

All of these representations of exposure can be nested within regression extensions for complex experimental designs such as repeated measures, crossover designs, or others.

Data from rat and dog exposure studies with CAPs are used to illustrate these statistical approaches; data from a human cohort, the Harvard Six Cities study, are also presented.

Results/Conclusions

Example using simple regression with heart and lung in vivo chemiluminescence (CL) data; Two rats were exposed to CAPs or filtered air for 6 hours each day; a total of 26 rats were assessed in each group on 13 different days.

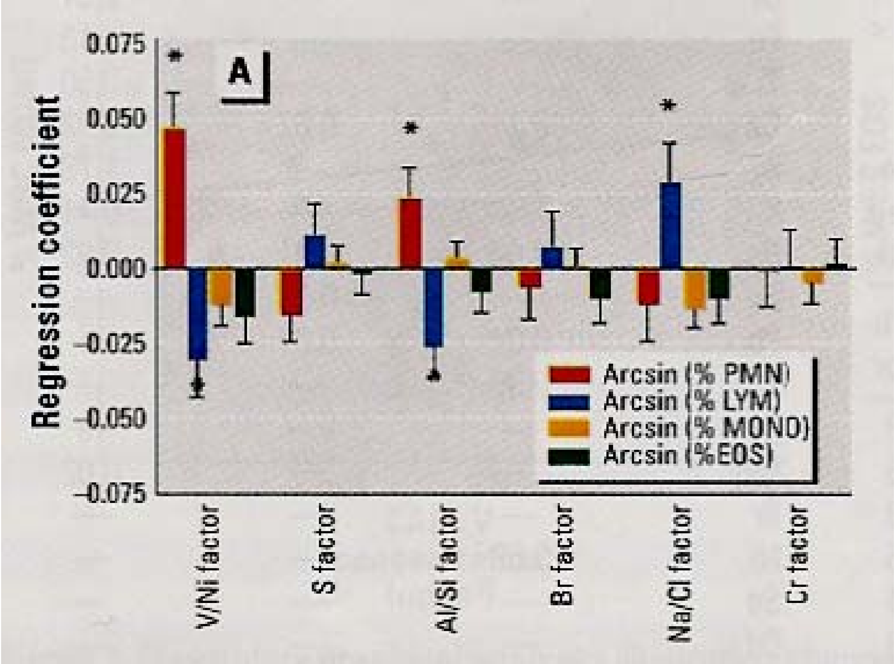
Element	Lung CL		Heart CL	
	r^2	p	r^2	p
Al	0.14	0.140	**0.67**	**0.001**
Si	0.31	0.020	**0.61**	**0.002**
S	0.14	0.140	0.08	0.360
Cl	0.14	0.070	0.08	0.360
K	0.39	0.008	0.30	0.500
Ca	0.41	0.007	0.36	0.030
Ti	0.38	0.008	**0.59**	**0.002**
V	0.02	0.620	0.42	0.020
Cr	0.04	0.440	0.32	0.046
Mn	**0.51**	**0.001**	0.43	0.010
Fe	**0.46**	**0.003**	**0.50**	**0.007**
Ni	0.00	0.840	0.27	0.070
Cu	**0.42**	**0.005**	0.29	0.060
Zn	**0.48**	**0.002**	0.38	0.020
As	0.31	0.020	0.08	0.340
Se	0.05	0.410	0.06	0.430
Br	0.24	0.040	0.13	0.230
Cd	0.01	0.680	0.38	0.030
Ba	0.36	0.011	0.22	0.110
Pb	0.31	0.020	0.38	0.020
Total mass	0.03	0.450	**0.51**	**0.003**

The most significant associations are indicated in bold.

Regression analyses of lung and heart CL with CAPs elemental components. Different elements have the strongest correlations with heart and lung responses. Metals are most strongly associated with CL in the lung; crustal elements associated with urban road dust are most strongly associated with CL in the heart.

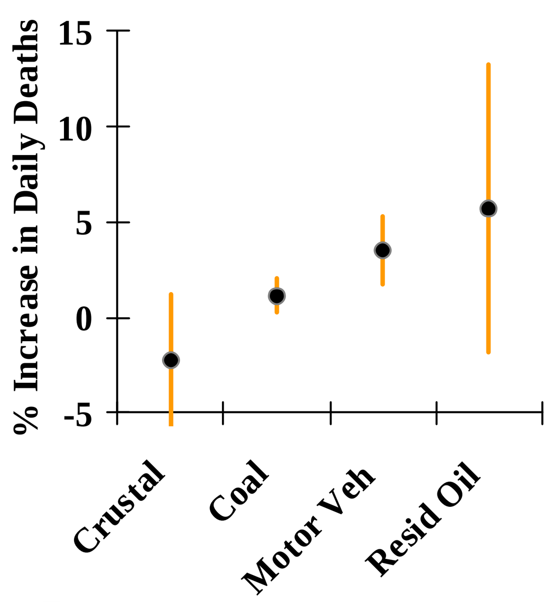
Examples using principle component analysis and source apportionment approaches

Regression values obtained by factor analysis of crossover exposure data compared to percentages of white blood cells. Data are controlled for individual dogs. Data represents 54 days of CAPs or Sham exposure of 10 different dogs. Note significant associations of increasing neutrophils with V/Ni and crustal/urban road dust factors.



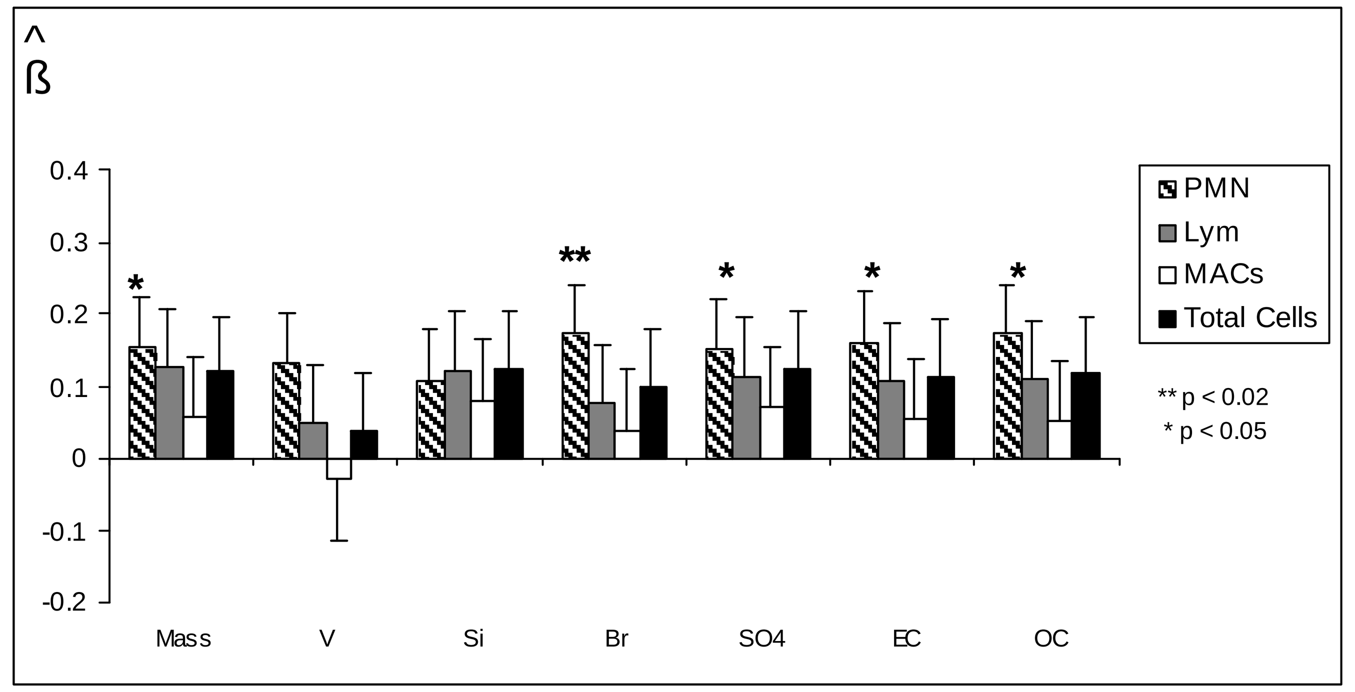
* p < 0.05

Source-Specific $PM_{2.5}$ and Daily Mortality in Six US Cities. Factor analysis of elemental composition of $PM_{2.5}$ used to estimate source-specific concentrations. Associations estimated with 4 source classes (10 $\mu g/m^3$)



Examples using the tracer method approach

Changes in Canine Breathing Patterns with exposure to CAPs using a multivariate model including sulfur, vanadium, silicon and sodium concentrations (12 dogs, 64 days of CAPs). Sulfur has the greatest effect on breathing pattern frequency and volumes, but these are physiological, not pathological changes. Vanadium effects pause, which may be an stronger indicator of pathology.



Examples using Semi-parametric modeling of complex exposure / component / response data.

Standardized regression coefficients for CAPs mass or component factor concentrations in relationship to BAL cellular changes in normal rats. A total of 50 normal Sprague Dawley rats were exposed on 18 different days. Significant associations with neutrophil increases are seen with mass and many source components.

Breathing Parameter	CAPs Component	Change	p
Frequency	sulfur	↑	0.004
Time Ins	sulfur	↓	0.015
Time Exp	sulfur	↓	0.020
Min Vol	sulfur	↑	0.027
End Exp Pau	vanadium	↑	0.015

Future Directions

- A major limitation of the approach described in this poster is that most individual studies have small numbers of exposures, which may limit the degrees of freedom for factor analyses.
- Studies are needed which combine large numbers of individual studies from one city so that more accurate source apportionment can be done. This analysis can then be applied in support of tracer elements in studies with smaller numbers of exposures.
- These approaches need to be used in a meta-analysis of all ambient particle concentrator studies done in various laboratories around the world.
- The statistical implications of using estimated (rather than known) source contributions of exposure also need to be assessed.

Impact and Outcomes

The studies and approach cited here have the capability to define source components and their toxicity in studies ranging from human epidemiology to large and small animal exposures. Insight from these studies is directly applicable in the control of specific sources.

Health and Exposure